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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/342,314	06/29/99	YELLIN M	C014CIP/DIV2

HM22/1023
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EXAMINER	
GAMBEL, P	

ART UNIT	PAPER NUMBER
1644	14

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 8/6/01

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1, 103 ~~-108~~, 108, 111 - 117, 130-131 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1, 103 - 108, 111-127, 130 - 131 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

DETAILED ACTION

1. Applicant's election of the species atherosclerosis is acknowledged.

Claims 1 and 103-129 are under consideration in the instant application

Claim 102 is withdrawn from further consideration as being drawn to the non-elected species.

2. In view of the applicant's Statement Deleting Inventors Under 37 CFR 1.63(d)(2), filed 6/29/99; the inventorship in this nonprovisional application has been changed by the deletion of David Thomas and Mihail Karpusas.

3.. The drawings filed 6/29/99 comply with comply with 37 CFR 1.84.

4. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Applicant is requested to clarify whether SEQ ID NO: 1 refers to Gly116-Leu261 or whether Gly116-Leu261 is embedded in SEQ ID NO: 1. See page 11, line 24 of the specification.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 128-129 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: wherein the methods to treat atherosclerosis (or accelerated atherosclerosis) wherein such methods encompass:
"administered with a gene therapy vector or a therapeutic agent" "wherein said therapeutic agent is an antigenic pharmaceutical or a blood product".

It is noted that page 27, paragraph 2 of the specification provides for the written support for coadministration of a compound of the invention along with a gene therapy vector or a therapeutic agent such as an antigenic pharmaceutical or a blood product in the specification as filed is in the context of preventing an immune response to an antigen and page 29, paragraph 3 of the specification provides written support for atherosclerosis (and accelerated atherosclerosis).

However, there appears to be insufficient written description as well as guidance and direction in the specification as filed for providing for these concepts together and, in particular, coadministration of a compound of the invention along with a gene therapy vector or a therapeutic agent as a dependent claim of treating atherosclerosis (and accelerated atherosclerosis).

The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to clarify the written support or direction for the dependent claim limitations in the context of treating atherosclerosis (and accelerated atherosclerosis).

8. Claims 128-129 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention essentially for the reasons.

It is noted that the instant claims are drawn to methods of treating atherosclerosis (and accelerated atherosclerosis).
It is noted that page 27, paragraph 2 of the specification as filed provides for the written support for coadministration of a compound of the invention along with a gene therapy vector or a therapeutic agent such as an antigenic pharmaceutical or a blood product in the specification as filed is in the context of preventing an immune response to an antigen and page 29, paragraph 3 of the specification provides written support for atherosclerosis (and accelerated atherosclerosis).

There appears to be insufficient guidance and direction in the specification as filed for providing for these concepts together and, in particular, coadministration of a compound of the invention along with a gene therapy vector or a therapeutic agent as a dependent claim of treating atherosclerosis (and accelerated atherosclerosis).

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of such "gene therapy vectors", "therapeutic agents". "antigenic pharmaceuticals" and "blood products" nor is there sufficient evidence provided how such "gene therapy vectors" , "therapeutic agents", "antigenic pharmaceutical" and "blood products" could be used in methods to "treat atherosclerosis (and accelerated atherosclerosis)". It would require undue experimentation to produce all such possible "gene therapy vectors", "therapeutic agents", "antigenic pharmaceutical" and "blood products" without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such "gene therapy vectors", "therapeutic agents", "antigenic pharmaceutical" and "blood products". It is not readily apparent from the claimed invention how these "gene therapy vectors", "therapeutic agents", "antigenic pharmaceuticals" and "blood products" are involved in the claimed methods to "treat atherosclerosis (and accelerated atherosclerosis)".

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods to "gene therapy vectors", "therapeutic agents", "antigenic pharmaceuticals" and "blood products". commensurate in scope with the claimed invention using the teaching of the specification.

9. Claims 1 and 103-129: It is apparent that the 5C8 antibodies/hybridoma is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

Given the availability of the 5C8 antibody produced by the hybridoma designated as ATCC HB 10916, as evidenced by U.S. Patent No. 5,474,771 (1449); the 5C8 antibody is considered enabled.

10. Claims 128-129 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention essentially for the reasons set forth in the previous Office Actions (Paper Nos. 22/25).

As pointed out above; it has been noted that page 27, paragraph 2 of the specification provides for the written support for coadministration of a compound of the invention along with a gene therapy vector or a therapeutic agent such as an antigenic pharmaceutical or a blood product in the specification as filed is in the context of preventing an immune response to an antigen and page 29, paragraph 3 of the specification provides written support for atherosclerosis (and accelerated atherosclerosis).

There appears to be insufficient guidance and direction in the specification as filed for providing for these concepts together and, in particular, coadministration of a compound of the invention along with a gene therapy vector or a therapeutic agent as a dependent claim of treating atherosclerosis (and accelerated atherosclerosis).

Therefore, the instant claims 132 and 133 are indefinite in the recitation of "administered with a gene therapy vector or a therapeutic agent" because the intention of the claim in the context of "treating atherosclerosis (and accelerated atherosclerosis)" is unclear.

Also, the characteristics of the "gene therapy vector", "therapeutic agent", antigenic pharmaceutical" and "blood products" are vague and indefinite since they encompass a myriad of different "vectors", "pharmaceuticals" "agents" and "products" and it is not apparent from the disclosure which particular "gene therapy vectors" , "therapeutic agents", "antigenic pharmaceuticals" and "blood products" are being referred to.

Applicant has not provided sufficient information that distinctly identifies the "gene therapy vector", "therapeutic agents", "antigenic pharmaceuticals" and "blood products" encompassed by the claimed methods to "treat atherosclerosis (and accelerated atherosclerosis)" .

The recitation of "gene therapy vector", "therapeutic agents", "antigenic pharmaceuticals" and "blood products" fails to distinctly claim what these molecules/compositions are or what they are made up of.

Therefore, there is insufficient information and guidance for the metes and bounds of the "gene therapy vectors", "therapeutic agents", "antigenic pharmaceuticals" and "blood products" encompassed by the claimed methods.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter

11 The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1 and 103-105, 109-117 and 128-129 are rejected under 35 U.S.C. § 102(e) as being anticipated by Wilson et al. (U.S. Patent No. 5,652,224). Wilson et al. teach the use of gene therapy vectors in combination with immunomodulators such as anti-CD40L antibodies (column 17, paragraph 4) to treat various disorders including atherosclerosis (see entire document, including Background of the Invention, and Detailed Description of the Invention).

It is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

With respect to the product-by-process limitations; the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) See MPEP 2113.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treating atherosclerosis with a gene therapy vector and the immunomodulator anti-CD40L antibody.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

14. Claims 1 and 103-129 are rejected under 35 U.S.C. § 103 as being unpatentable over Wilson et al. (U.S. Patent No. 5,652,224) in view of art known methods of generating modified antibodies of interest, as acknowledged by applicant on pages 13-15 of the instant specification and in view of Lederman et al. (WO 93/09812; 1449.

Wilson et al. teach the use of gene therapy vectors in combination with immunomodulators such as anti-CD40L antibodies (column 17, paragraph 4) to treat various disorders including atherosclerosis (see entire document, including Background of the Invention, and Detailed Description of the Invention).

Lederman et al.(WO 93/09812) teach the inhibition of various immune cell interactions associated with 5C8 via 5C8-specific antibodies, including recombinant antibodies and methods of screening for said antibodies (see entire document) The referenced 5C8 antigen specificity was also known as CD40L at the time this publication was available

Given the teachings that the immunomodulator anti-CD40L antibodies would be beneficial in the treatment of atherosclerosis and the teachings that 5C8-/CD40L-specific antibodies affect a number of cell interactions; the claimed effects on transmigration, blood vessels, endothelial cells and smooth muscle cells would have been expected given the ability to inhibit CD40L-mediated responses including the inhibition of atherosclerosis.

It was well known and practiced at the time the invention was made to make and modify antibodies for human use, including the generation of various antigen-binding fragments (e.g. Fab, single chain antibody) as well as recombinant antibodies (e.g. chimeric, humanized and primatized) encompassed by the claimed methods. It was art known methods to employ recombinant forms of antibodies to increase half-life and efficacy of antibody-mediated therapies and to screen antibodies of interest.

It was well known and practiced at the time the invention was made that treating atherosclerosis required the administration of other therapeutic agents. Although CD40L-specific antibodies could be used to inhibit the response to the gene therapy vector; the reliance on conventional therapeutic intervention in combination therapies as well as additional therapeutic agents was known and required at the time the invention was made. In addition, given the breath of therapeutic agents/blood products; this limitations would have been met by the administration of conventional therapeutic intervention in the treatment of atherosclerosis at the time the invention was made.

In addition to the teachings above; the claimed dosages and routes of administration were known and practiced at the time the invention was made and/or would have been encompassed in providing for sufficient therapeutic intervention depending on the patient's needs at the time the invention was made.

Therefore, the combined teachings teach targeted inflammatory conditions including those that involve the treatment of atherosclerosis by inhibiting CD40-CD40L interactions with CD40L-specific antibodies. It was known at the time the invention was made to employ recombinant antibodies and antibody fragments to increase half-life and efficacy of antibody-mediated therapies. Also, the generation of recombinant antibodies such as chimeric, humanized and primatized as well as standard antibody screening procedures as well as modes of administration were all well known in the art at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to select the ability of CD40L-specific antibodies in combination with a gene therapy to inhibit atherosclerosis. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
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Technology Center 1600
March 29, 2001